【Grant-in-Aid for Scientific Research (S)】

Integrated Disciplines (Complex Systems)

Title of Project : Development of Neo-Bionanocapsules: Drug and Gene Delivery System to Wide Range Tissues with Virus-derived Functional Domains

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Research Project Number : 16H06314 Researcher Number : 60263406
Research Area : Drug Delivery System
Keyword : Nanomedicine, Virus, Automated Single-cell Analysis and Isolation System

【Purpose and Background of the Research】

Conventional synthetic nanocarriers for drug delivery system (DDS) have hardly accomplished to harbor the following three functions simultaneously: *in vivo* active targeting ability, stealth ability for escaping from immune system, and cell entering ability. We have focused on hepatitis B virus (HBV) envelope L protein, indispensable for human liver-specific infection, and then generated bio-nanocapsule (BNC) by expressing L protein in yeast cells. So far, we have demonstrated that BNC functions as a human liver-specific DDS nanocarrier by the above three abilities in the ectodomain of L protein (Figure 1).

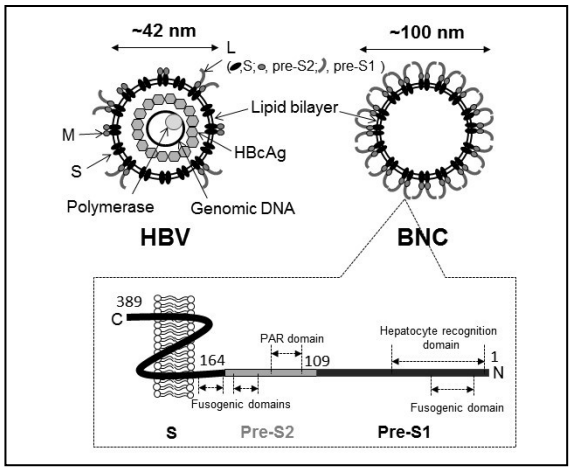

Figure 1 HBV, BNC, and Their Domains

Considering the use of BNC as a forthcoming DDS nanocarrier in clinical sites, it is very hard to produce BNC under current good manufacturing practice (GMP), because BNC is a hybrid of chemical drug and biological drug. In this project, we will reconstitute the above three abilities on the conventional synthetic DDS nanocarriers (e.g., liposomes, nanomicelles) by using chemically defined materials exclusively.

【Research Methods】

In FY2016, we will develop short peptides exhibiting stealth ability and cell entering ability, which show equal activity of HBV. Meanwhile, we will establish affibodies recognizing various tissues and cells (including cancers) specifically by using an automated single-cell analysis and isolation system (our original robot). After FY2017, we will elucidate the mechanism how the peptides with stealth ability and cell entering ability work on the molecular basis. Furthermore, we will optimize the immobilization of affibody, stealth peptide, and cell entering peptide on the conventional synthetic DDS nanocarriers by the realtime observation under high-speed atomic force microscopy (our original method). Finally, we will obtain versatile "Neo-BNC" consisting of chemically defined materials exclusively, which harbors stringent and strong *in vivo* active targeting ability, strong stealth ability without using polymers, and efficient cell entering ability.

【Expected Research Achievements and Scientific Significance】

Neo-BNC will contribute to the development of forthcoming nanomedicines as a platform technology. Especially, the issues occurred in current RNA medicines will be addressed.

【Publications Relevant to the Project】

Nanoparticles for the Delivery of Genes and Drugs to Human Hepatocytes. Yamada T, et al., Nature Biotechnol. 21 (2003) 885-890.
Development of a Virus-mimicking Nanocarrier for Drug Delivery Systems: The bio-nanocapsule. Somiya M, and Kuroda S. Adv. Drug Delivery Rev. 95 (2015) 77-89.

【Term of Project】 FY2016-2020

【Budget Allocation】 139,100 Thousand Yen

【Homepage Address and Other Contact Information】

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